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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/820,622	04/08/2004	Susan F. Radka	02-030-B (900.051)	8184

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MCDONNELL, BOEHNEN, HULBERT AND BERGHOFF, LLP
300 SOUTH WACKER DRIVE
SUITE 3100
CHICAGO, IL 60606

EXAMINER	
BLANCHARD, DAVID J	
ART UNIT	**PAPER NUMBER**
1643	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/820,622	RADKA, SUSAN F.	
	Examiner	Art Unit	
	David J. Blanchard	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 April 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-29* is/are pending in the application.

4a) Of the above claim(s) *15-29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *08 April 2004 and 27 September 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/19/04; 10/22/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The preliminary amendment filed 27 September 2004 has been entered in full.

2. Claims 1-29 are pending.

Election/Restrictions

3. Applicant's election of Group I, claims 1-14 in the reply filed on 23 April 2007 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Applicants request for rejoinder is acknowledged. Applicants' attention is directed to MPEP 821.04.

4. Claims 15-29 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention.

5. Claims 1-14 are under consideration.

Specification

6. The disclosure is objected to because of the following informalities:

a. The first line of the specification needs to be updated with the U.S. patent number for USSN 10/366,191, filed 2/12/2003. The patent number is U.S. Patent 7,071,311.

b. The specification references other US Patent Application numbers, whose status has changed since the filing of the present application. For example, see page 7, par. 0014, page 14, par. 0035, page 16, par. 0042, and page 61, par. 0170. USSNs 10/720,448 and 10/201,394 are "now abandoned" and USSN 10/151,116 is now US Patent 7,109,165. The status of USSN 10/665,951 should be updated during the pendency of the instant application, as necessary. Applicant's cooperation is requested in reviewing the entire disclosure for additional US Application serial numbers that require updating.

c. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

8. Claims 2-5 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 2-5 are indefinite in the recitation "comprises a short interfering nucleic acid (siNA)" in claim 2. Does the nucleic acid having a 2'-deoxy-2'-fluoro Uridine nucleoside and/or nucleotide comprise a siNA or is it the siNA. Is the siNA linked to a nucleic acid molecule having a 2'-deoxy-2'-fluoro Uridine nucleoside and/or nucleotide? One of skill in the art would not know whether the siNA is the nucleic acid having a 2'-deoxy-2'-fluoro Uridine nucleoside and/or nucleotide or is in addition to a nucleic acid having a 2'-deoxy-2'-fluoro Uridine nucleoside and/or nucleotide.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 1-6 are rejected under 35 U.S.C. 102(b) as being anticipated by Reines (Analytical Biochemistry, 196(2):367-372, 1991 Aug 1).

The claims are drawn to an isolated antibody or monoclonal antibody having binding affinity for a nucleic acid molecule having a 2'-deoxy-2'-C-fluoro Uridine nucleoside and/or nucleotide, wherein said nucleic acid is a siNA, a duplex siNA, a hairpin siNA and wherein the 2'-deoxy-2'-C-fluoro Uridine nucleoside and/or nucleotide is on one or both strands of said duplex siNA. Applicant is reminded that the term "comprising" is inclusive or open-ended and does not exclude additional unrecited

elements. See MPEP 2111.03. Further, in light of the specification the term "having" is interpreted as open-ended, i.e., equivalent to "comprising" and thus, does not exclude additional unrecited elements.

Reines teaches an isolated murine monoclonal antibody specific for RNAs of differing size and nucleotide sequence and is an isolated antibody that would necessarily bind a nucleic acid molecule having a 2'-deoxy-2'-fluoro Uridine nucleoside and/or nucleotide and would necessarily bind a siNA, a duplex siNA, and a hairpin siNA comprising a 2'-deoxy-2'-C-fluoro Uridine nucleoside and/or nucleotide. The claims do not require any particular antibody specificity, such as the recognition of the unique structures of the present claims, nor do the claims exclude additional sequence from the specifically recited sequences (i.e., "comprising" and "having"). Thus, an antibody which binds to sequence upstream or downstream of the unique structures of the present claims reads upon the claims.

Thus, Reines anticipates the claims.

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 1-9 and 12-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Reynaud et al, Cancer Letters, 61(3):255-262, January 31, 1992) in view of Kawasaki et al, J. Med. Chem., 36(7):831-841, April 2, 1993).

Reynaud et al teach monoclonal antibodies specific for modified nucleosides for the detection of nucleoside modifications in patients and a method for producing the monoclonal antibodies comprising conjugating the modified nucleoside to a carrier (bovine serum albumin), immunizing mice with the conjugate, fusing splenic lymphocytes with plasmacytoma cells and isolating the monoclonal antibodies from the hybridoma supernatant (see entire document, particularly pg. 256). Reynaud et al do not specifically teach a monoclonal antibody having specificity for a 2'-deoxy-2'-C-fluoro Uridine nucleoside and/or nucleotide of a short interfering nucleic acid (siNA) or antisense molecule or a method of making said monoclonal antibody. This deficiency is made up for in the teachings of Kawasaki et al.

Kawasaki et al teach antisense molecules comprising uniformly modified 2'-deoxy-2'-fluoro uridine that have high binding affinity and selectivity for the RNA target and are stable against nucleases (see entire document).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to have produced an antibody having affinity for a 2'-deoxy-2'-fluoro uridine nucleoside/nucleotide of an siNA and a method of making said monoclonal antibody according to the method of Reynaud et al for detecting the siNA in antisense patients.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success at the time the invention was made to have produced an antibody having affinity for a 2'-deoxy-2'-fluoro uridine nucleoside/nucleotide of an siNA and a method of making said monoclonal antibody according to the method of Reynaud et al for detecting the siNA in antisense patients in view of Reynaud et al and Kawasaki et al because Reynaud et al teach monoclonal antibodies specific for modified nucleosides for the detection of nucleoside modifications in patients and a method for producing the monoclonal antibodies comprising conjugating the modified nucleoside to a carrier (bovine serum albumin), immunizing mice with the conjugate, fusing splenic lymphocytes with plasmacytoma cells and isolating the monoclonal antibodies from the hybridoma supernatant and Kawasaki et al teach antisense molecules (i.e., siNA's) comprising uniformly modified 2'-deoxy-2'-fluoro uridine have high binding affinity and selectivity for the RNA target and are stable against nucleases. Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to have produced antisense molecules comprising uniformly modified 2'-deoxy-2'-fluoro uridine that are advantagous for antisense technology since they have high binding affinity and selectivity for the RNA target and are stable against nucleases and one of ordinary skill in the art would have been motivated to have produced monoclonal antibodies specific for the 2'-deoxy-2'-fluoro uridine nucleoside/nucleotide as taught by Reynaud et al for detection of the 2'-deoxy-2'-fluoro uridine antisense molecules following administration in antisense patients. Thus, it would have been *prima facie* obvious to one skilled in the art at the time the invention was made to have produced an antibody having affinity for a 2'-deoxy-2'-fluoro uridine nucleoside/nucleotide of an siNA and a method of making said monoclonal antibody according to the method of Reynaud et al for detecting the siNA in antisense patients in view of Reynaud et al and Kawasaki et al.

Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Double Patenting

13. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

14. Claims 1-14 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 and 6-8 of U.S. Patent No. 7,071,311 in view of Kawasaki et al (J. Med. Chem., 36(7):831-841, April 2, 1993).

The instant claims are drawn to an isolated antibody or monoclonal antibody having binding affinity for a nucleic acid molecule having a 2'-deoxy-2'-C-fluoro Uridine nucleoside and/or nucleotide, wherein said nucleic acid is a siNA, a duplex siNA, a hairpin siNA and wherein the 2'-deoxy-2'-C-fluoro Uridine nucleoside and/or nucleotide is on one or both strands of said duplex siNA and a method for generating a monoclonal antibody having binding affinity for nucleic acid molecules having a 2'-deoxy-2'-fluoro Uridine nucleoside or nucleotide comprising conjugating a polynucleotide having a 2'-deoxy-2'-fluoro Uridine nucleoside or nucleotide to a carrier protein to form a polynucleotide-protein conjugate, immunizing a mammal with the conjugate, obtaining antibody producing cells from the mammal, fusing said antibody producing cells with a

myeloma cell under conditions suitable for generating a hybridoma and using the supernatant from the hybridoma in a fusion screen for isolating the monoclonal antibody and wherein the mammal is a mouse and the 2'-deoxy-2'-fluoro Uridine polynucleotide is biotinylated, is a siNA, is a duplex siNA, or is a hairpin siNA.

Claims 1 and 6-8 of U.S. Patent No. 7,071,311 are drawn to an isolated monoclonal antibody having binding affinity for a 2'-deoxy-2'-C-allyl Uridine nucleoside or 2'-deoxy-2'-C-allyl Uridine nucleotide of a nucleic acid molecule, wherein the monoclonal antibody is a murine IgGk antibody and a method for generating a monoclonal antibody having the binding affinity of claim 1, the method comprising: (a) Conjugating a 2'-deoxy-2'-C-allyl Uridine nucleotide to a carrier protein, to form a nucleotide-protein conjugate; (b) Immunizing a SJL mouse the conjugate from (a); (c) Obtaining antibody producing cells from the immunized SJL mouse (b); (d) Fusing cells obtained from the SJL mouse of (b) with a myeloma cell under conditions suitable for generating a hybridoma; and (e) using supernatant from the hybridoma of (d) in a fusion screen under conditions suitable for isolating the monoclonal antibody and wherein the 2'-deoxy-2'-C-ally Uridine nucleotide of (a) is a 2'-deoxy-2'-C-allyl Uridine 5'-phosphate. Claims 1 and 6-8 of U.S. Patent No. 7,071,311 do not teach an isolated monoclonal antibody having binding affinity for a nucleic acid molecule having a 2'-deoxy-2'-C-fluoro Uridine nucleoside and/or nucleotide or a method of method for generating a monoclonal antibody having binding affinity for nucleic acid molecules having a 2'-deoxy-2'-fluoro Uridine nucleoside or nucleotide comprising conjugating a polynucleotide having a 2'-deoxy-2'-fluoro Uridine nucleoside or nucleotide to a carrier protein to form a polynucleotide-protein conjugate, immunizing a mammal with the conjugate, obtaining antibody producing cells from the mammal, fusing said antibody producing cells with a myeloma cell under conditions suitable for generating a hybridoma and using the supernatant from the hybridoma in a fusion screen for isolating the monoclonal antibody. Theses deficiencies are made up for in the teachings of Kawasaki et al.

Kawasaki et al have been described supra.

The claims in the instant application are obvious variants of claims 1 and 6-8 of U.S. Patent No. 7,071,311 because it would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to have produced an antibody having affinity for a 2'-deoxy-2'-fluoro uridine nucleotide of an antisense molecule.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have produced an antibody having affinity for a 2'-deoxy-2'-fluoro uridine nucleotide of an antisense molecule in view of claims 1 and 6-8 of U.S. Patent No. 7,071,311 and Kawasaki et al because claim 1 and 6-8 teach a monoclonal antibody having binding affinity for a modified nucleotide of an siNA molecule and a method of making the monoclonal antibody and Kawasaki et al teach antisense molecules (i.e., siNA) uniformly modified 2'-deoxy-2'-fluoro uridine have high binding affinity and selectivity for the RNA target and are stable against nucleases. Thus, there would be an advantage to using siNA's uniformly modified 2'-deoxy-2'-fluoro uridine for therapy and hence, a monoclonal antibody having affinity for the 2'-deoxy-2'-fluoro uridine nucleotide of the siNA's. Thus, it would have been *prima facie* obvious to one of ordinary skill in the art success to have produced an antibody having affinity for a 2'-deoxy-2'-fluoro uridine nucleotide of an antisense molecule in view of claims 1 and 6-8 of U.S. Patent No. 7,071,311 and Kawasaki et al.

Claims 1-14 are directed to an invention not patentably distinct from claims 1 and 6-8 of commonly assigned U.S. Patent No. 7,071,311. Specifically, see above.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP Chapter 2300). Commonly assigned U.S. Patent No. 7,071,311, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions

were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications pending on or after December 10, 2004.

This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

15. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Blanchard whose telephone number is (571) 272-0827. The examiner can normally be reached at Monday through Friday from 8:00 AM to 6:00 PM, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached at (571) 272-0832.

The official fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/David J. Blanchard/
Primary Examiner, A.U. 1643